



1/48

ATGGCCCAAGCCCTGCCCTGGCTCCTGCTGTGGATGGGCGCGGGAG  
TGCTGCCTGCCACGGCACCCAGCACGGCATCCGGCTGCCCCCTGCG  
CAGCGGCCTGGGGGGCGCCCCCTGGGGCTGCGGCTGCCCCGGGA  
GACCGACGAAGAGCCCCGAGGAGCCCGGCCGGAGGGGCGAGCTTTGT  
GGAGATGGTGGACAACCTGAGGGGGCAAGTCGGGGCAGGGCTACTAC  
GTGGAGATGACCGTGGGCAGCCCCCGCAGACGCTCAACATCCTGG  
TGGATACAGGCAGCAGTAACTTTGCAGTGGGTGCTGCCCCCACCC  
CTTCCTGCATCGCTACTACCAGAGGCAGCTGTCCAGCACATACCGGG  
ACCTCCGGAAGGGTGTGTATGTGCCCTACACCCAGGGCAAGTGGGA  
AGGGGAGCTGGGCACCGACCTGGTAAGCATCCCCCATGGCCCCAAC  
GTCATGTGCGTGCCAACATTGCTGCCATCACTGAATCAGACAAGTT  
CTTCATCAACGGCTCCAACCTGGGAAGGCATCCTGGGGCTGGCCTATG  
CTGAGATTGCCAGGCCTGACGACTCCCTGGAGCCTTTCTTTGACTCT  
CTGGTAAAGCAGACCCACGTTCCCAACCTCTTCTCCCTGCAGCTTTG  
TGGTGCTGGCTTCCCCCTCAACCAGTCTGAAGTGCTGGCCTCTGTCG  
GAGGGAGCATGATCATTGGAGGTATCGACCACTCGCTGTACACAGGC  
AGTCTCTGGTATACACCCATCCGGCGGGAGTGGTATTATGAGGTGAT  
CATTGTGCGGGTGGAGATCAATGGACAGGATCTGAAAATGGACTGCA  
AGGAGTACAACCTATGACAAGAGCATTGTGGACAGTGGCACCACCAAC  
CTTCGTTTGCCCAAGAAAGTGTGTTGAAGCTGCAGTCAAATCCATCAAG  
GCAGCCTCCTCCACGGAGAAGTTCCCTGATGGTTTCTGGCTAGGAGA  
GCAGCTGGTGTGCTGGCAAGCAGGCACCACCCCTTGGAACATTTTCC  
CAGTCATCTCACTCTACCTAATGGGTGAGGTTACCAACCAGTCCTTCC  
GCATCACCATCCTTCCGCAGCAATACCTGCGGCCAGTGGGAAGATGTG  
GCCACGTCCCAAGACGACTGTTACAAGTTTGCCATCTCACAGTCATC  
CACGGGCACTGTTATGGGAGCTGTTATCATGGAGGGCTTCTACGTTG  
TCTTTGATCGGGCCCGAAAACGAATTGGCTTTGCTGTCAGCGCTTGC  
CATGTGCACGATGAGTTCAGGACGGCAGCGGTGGAAGGCCCTTTTG  
TCACCTTGGACATGGAAGACTGTGGCTACAACATTCCACAGACAGAT  
GAGTCAACCCTCATGACCATAGCCTATGTCATGGCTGCCATCTGCGC  
CCTCTTCATGCTGCCACTCTGCCTCATGGTGTGTGAGTGGCGCTGCC  
TCCGCTGCCTGCGCCAGCAGCATGATGACTTTGCTGATGACATCTCC  
CTGCTGAAG

FIG. 1A



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CCATGCCGGCCCCCTCACAGCCCCGCCGGGAGCCCCGAGCCCCGCTGCCCAGG  
 CTGGCCGCCGCSGTGCCGATGTAGCGGGCTCCGGATCCCAGCCTCTCCCCCT  
 GCTCCCGTGCTCTGCGGATCTCCCCTGACCGCTCTCCACAGCCCCGGACCCG  
 GGGGCTGGCCCAGGGCCCTGCAGGCCCTGGCGTCCTGATGCCCCCAAGCT  
 CCCTCTCCTGAGAAGCCACCAGCACCCAGACTTGGGGGCAGGCGCCA  
 GGGACGGACGTGGGCCAGTGCGAGCCCAGAGGGGCCCGAAGGCCGGGGCC  
 CACCATGGCCCAAGCCCTGCCCTGGCTCCTGCTGTGGATGGGCGCGGGAG  
 TGCTGCCTGCCCACGGCACCCAGCACGGCATCCGGCTGCCCTGCGCAGC  
 GGCCTGGGGGGCGCCCCCTGGGGCTGCGGCTGCCCCGGGAGACCGACG  
 AAGAGCCCCGAGGAGCCCCGGCCGGAGGGGCAGCTTTGTGGAGATGGTGGAC  
 AACCTGAGGGGCAAGTCGGGGCAGGGCTACTACGTGGAGATGACCGTGGG  
 CAGCCCCCGCAGACGCTCAACATCCTGGTGGATACAGGCAGCAGTAACTT  
 TGCAGTGGGTGCTGCCCCCACCCCTTCCTGCATCGCTACTACCAGAGGCA  
 GCTGTCCAGCACATAACGGGACCTCCGGAAGGGTGTGTATGTGCCCTACAC  
 CCAGGGGCAAGTGGGAAGGGGAGCTGGGCACCGACCTGGTAAGCATCCCCC  
 ATGGCCCCAACGTCACTGTGCGTGCCAACATTGCTGCCATCACTGAATCAGA  
 CAAGTTCTTCATCAACGGCTCCAACCTGGGAAGGCATCCTGGGGCTGGCCTAT  
 GCTGAGATTGCCAGGCCTGACGACTCCCTGGAGCCTTTCTTTGACTCTCTGG  
 TAAAGCAGACCCACGTTCCCAACCTCTTCTCCCTGCAGCTTTGTGGTGCTGG  
 CTTCCCCCTCAACCAGTCTGAAGTGCTGGCCTCTGTGCGAGGGGAGCATGAT  
 CATTGGAGGTATCGACCACTCGCTGTACACAGGCAGTCTCTGGTATACACCC  
 ATCCGGCGGGAGTGGTATTATGAGGTGATCATTGTGCGGGTGGAGATCAAT  
 GGACAGGATCTGAAAATGGACTGCAAGGAGTACAACCTATGACAAGAGCATTG  
 TGGACAGTGGCACCACCAACCTTCGTTTGCCCCAAGAAAGTGTTTGAAGCTGC  
 AGTCAAATCCATCAAGGCAGCCTCCTCCACGGAGAAGTTCCCTGATGGTTTC  
 TGGCTAGGAGAGCAGCTGGTGTGCTGGCAAGCAGGCACCACCCCTTGGAAC  
 ATTTTCCCAGTCATCTCACTCTACCTAATGGGTGAGGTTACCAACCAGTCCTT  
 CCGCATCACCATCCTTCCGCAGCAATACCTGCGGCCAGTGGAAGATGTGGC  
 CACGTCCCAAGACGACTGTTACAAGTTTGCCATCTCACAGTCATCCACGGGC  
 ACTGTTATGGGAGCTGTTATCATGGAGGGCTTCTACGTTGTCTTTGATCGGG  
 CCCGAAAACGAATTGGCTTTGCTGTGACGCGCTTGCCATGTGCACGATGAGTT  
 CAGGACGGCAGCGGTGGAAGGCCCTTTTGTACCTTGGACATGGAAGACTG  
 TGGCTACAACATTCCACAGACAGATGAGTCAACCCTCATGACCATAGCCTAT  
 GTCATGGCTGCCATCTGCGCCCTCTTCATGCTGCCACTCTGCCTCATGGTGT  
 GTCAGTGGCGCTGCCTCCGCTGCCTGCGCCAGCAGCATGATGACTTTGCTG  
 ATGACATCTCCCTGCTGAAGTGAGGAGGCCCATGGGCAGAAGATAGAGATT  
 CCCCTGGACCACACCTCCGTGGTTCACTTTGGTCACAAGTAGGAGACACAGA  
 TGGCACCTGTGGCCAGAGCACCTCAGGACCCTCCCCACCCACCAAATGCCT  
 CTGCCCTTGATGGAGAAGGAAAAGGCTGGCAAGGTGGGTTCCAGGGACTGTA  
 CCTGTAGGAAACAGAAAAGAGAAGAAAGAAGCACTCTGCTGGCGGGGAATAC  
 TCTTGGTCACCTCAAATTTAAGTCGGGAAATTCTGCTGCTTGAAACTTCAGCC  
 CTGAACCTTTGTCCACCATTCCTTTAAATTCTCCAACCCAAAGTATTCTTCTTT  
 TCTTAGTTTCAGAAGTACTGGCATCACACGCAGGTTACCTTGGCGTGTGTCC  
 CTGTGGTACCCTGGCAGAGAAGAGACCAAGCTTGTTTCCCTGCTGGCCAAA  
 GTCAGTAGGAGAGGATGCACAGTTTGCTATTTGCTTTAGAGACAGGGACTGT  
 ATAAACAAGCCTAACATTGGTGCAAGATTGCCTCTTGAATT

FIG. 1B



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MAQALPWLLLWMGAGVLP AHGTQHGIRLPLRSGLG GAPLGLRL  
PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYYVEMTVGSPP  
QTLNILVDTGSSNFAVGAAPHPFLHRYYQRQLSSTYRDLRKGVY  
VPYTQGKWEDELGTDLVSIPHGPNTVRANIAAITESDKFFINGS  
NWEGLGLAYAEIARPDDSLEPFFDSL VKQTHVPNLFSLQLCGAG  
FPLNQSEVLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYYEVIIV  
RVEINGQDLKMDCKEYNYDKSIVDSGTTNLRLPKKVFEAAVKSIIK  
AASSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTN  
QSFRITILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIM  
EGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDC  
GYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLR  
QQHDDFADDISLLK

FIG. 2A



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ETDEEPEEPGRRGSFVEMVDNLRGKSGQGYYVEMTVGSPQT  
LNILVDTGSSNFAVGAAPHPFLHRYRQRQLSSTYRDLRKGYYVP  
YTQGWEGELGTDLVSIHPGNVTVRANIAAITESDKFFINGSNW  
EGILGLAYAEIARPDDSLPFFDSLVKQTHVPNLFSLQLCGAGFP  
LNQSEVLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYYEVIIVRV  
EINGQDLKMDCKEYNYDKSIVDSGTTNLRLPKKVFEEAAVKSIAA  
SSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTNQ  
SFRITILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIME  
GFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDC  
GYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLR  
QQHDDFADDISLLK

FIG. 2B



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MAQALPWLLLWMGAGVLP AHGTQH GIRLPLRSG LGGAPLGLRL  
PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYYVEMTVGSPP  
QTLNILVDTGSSNFAVGAAPHPFLHRYYYQRQLSSTYRDLRKGVY  
VPYTQGKWE GELGTDLV SIPHGPNVTVRANIAAITESDKFFINGS  
NWE GILGLAYAEIARPDDSLEPFFDSL VKQTHVPNLFSLQLCGAG  
FPLNQSEVLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYYEVIIV  
RVEINGQDLKMDCKEYNYDKSIVDSGTTNLRLPKKVFEAAVKSIIK  
AASSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTN  
QSFRITILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIM  
EGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDC  
GYNIPQTDEDYKDDDDK

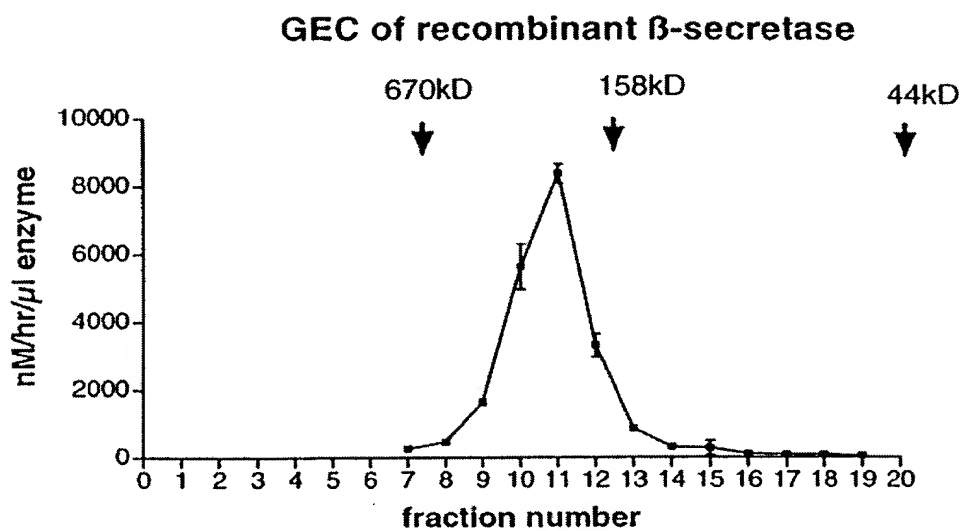
FIG. 3A

ETDEEPEEPGRRGSFVEMVDNLRGKSGQGYYVEMTVGSPPQT  
LNILVDTGSSNFAVGAAPHPFLHRYYYQRQLSSTYRDLRKGVYVP  
YTQGKWE GELGTDLV SIPHGPNVTVRANIAAITESDKFFINGSNW  
EGILGLAYAEIARPDDSLEPFFDSL VKQTHVPNLFSLQLCGAGFP  
LNQSEVLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYYEVIIVRV  
EINGQDLKMDCKEYNYDKSIVDSGTTNLRLPKKVFEAAVKSIIKAA  
SSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTNQ  
SFRITILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIME  
GFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDC  
GYNIPQTDEDYKDDDDK

FIG. 3B



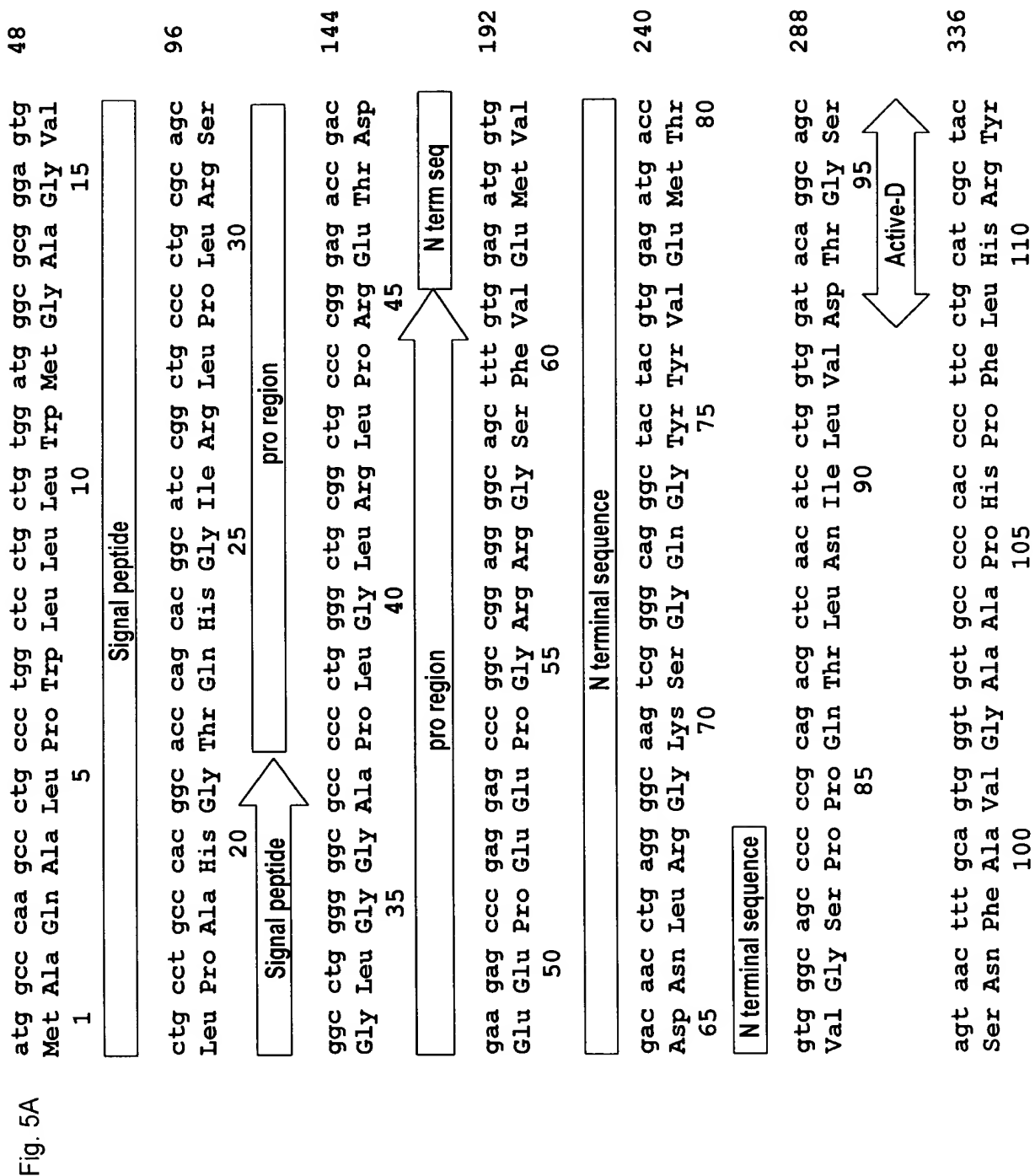
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**FIG. 4**



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## Replacement Sheet





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Fig. 5C

tct gaa gtg ctg gcc tct gtc gga ggg agc atg atc att gga ggt atc 720  
Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile  
225 230 235 240


**N-gly**

gac cac tcg ctg tac aca ggc agt ctg tgg tat aca ccc atc cgg cgg 768  
Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg  
245 250 255

gag tgg tat tat gag gtg atc att gtg cgg gtg gag atc aat gga cag 816  
Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln  
260 265 270

gat ctg aaa atg gac tgc aag gag tac aac tat gac aag agc att gtg 864  
Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val  
275 280 285

gac agt ggc acc acc aac ctt cgt ttg ccc aag aaa gtg ttt gaa gct 912  
Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala  
290 295 300

 Active-D

gca gtc aaa tcc atc aag gca gcc tcc tcc acg gag aag ttc cct gat 960  
Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp  
305 310 315 320

ggt ttc tgg cta gga gag cag ctg gtg tgc tgg caa gca ggc acc acc 1008  
Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr  
325 330 335



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Fig. 5D

cct tgg aac att ttc cca gtc atc tca ctc tac cta atg ggt gag gtt Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val 340 345 350	1056
acc aac cag tcc ttc cgc atc acc atc ctt ccg cag caa tac ctg cgg Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg 355 360 365	1104
N-glycos	
cca gtg gaa gat gtg gcc acg tcc caa gac gac tgt tac aag ttt gcc Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala 370 375 380	1152
atc tca cag tca tcc acg ggc act gtt atg gga gct gtt atc atg gag Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu 385 390 395 400	1200
ggc ttc tac gtt gtc ttt gat cgg gcc cga aaa cga att ggc ttt gct Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala 405 410 415	1248
gtc agc gct tgc cat gtg cac gat gag ttc agg acg gca gcg gtg gaa Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu 420 425 430	1296
Internal peptide sequence	



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Fig. 5E 1344

ggc cct ttt gtc acc ttg gac atg gaa gac tgt ggc tac aac att cca  
Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro  
435 440 445

1392

cag aca gat gag tca acc ctc atg acc ata gcc tat gtc atg gct gcc  
Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala  
450 455 460

Transmembrane

1440

atc tgc gcc ctc ttc atg ctg cca ctc tgc ctc atg gtg tgt cag tgg  
Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp  
465 470 475 480

Transmembrane

1488

cgc tgc ctc cgc tgc ctg cgc cag cag cat gat gac ttt gct gat gac  
Arg Cys Leu Arg Cys Leu Arg Gln His Asp Asp Phe Ala Asp Asp  
485 490 495

1506

atc tcc ctg ctg aag tga  
Ile Ser Leu Leu Lys  
500



# Replacement Sheet

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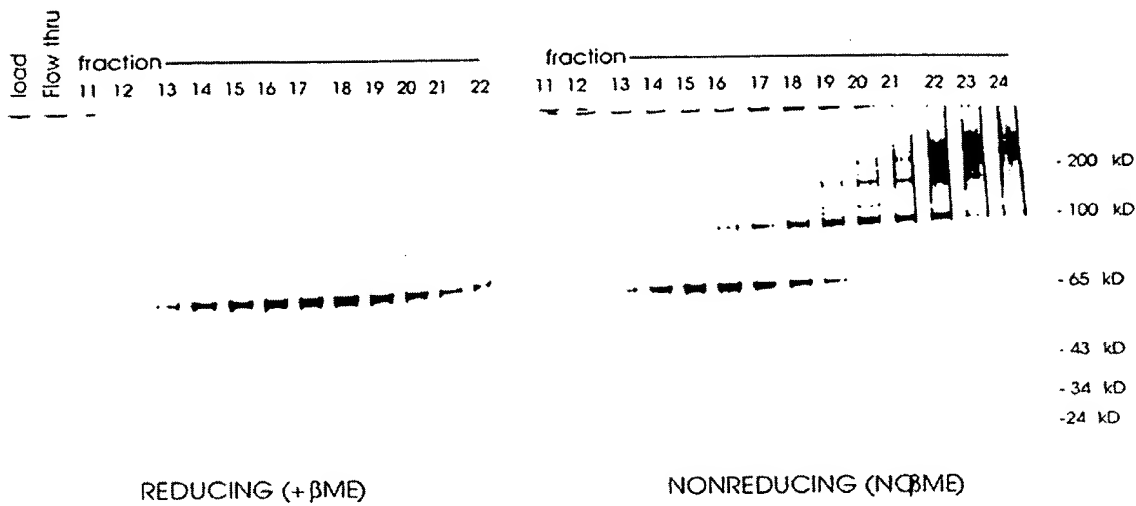


FIG. 6A

FIG. 6B



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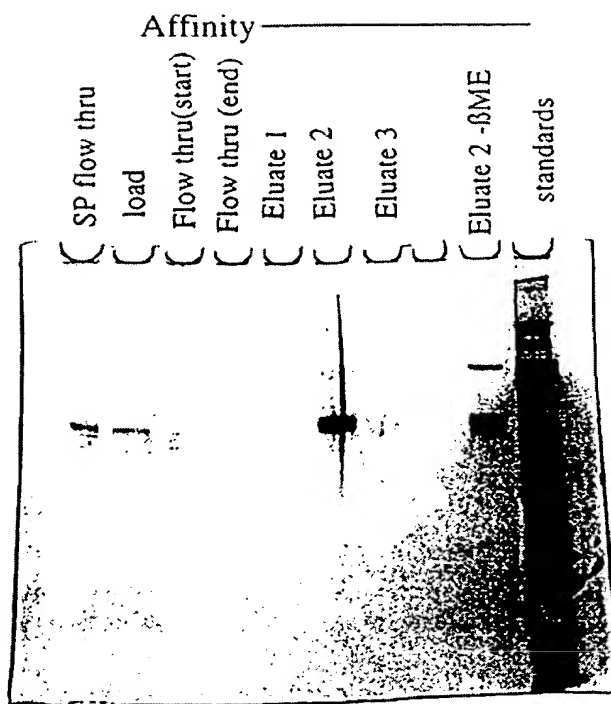


FIG. 7

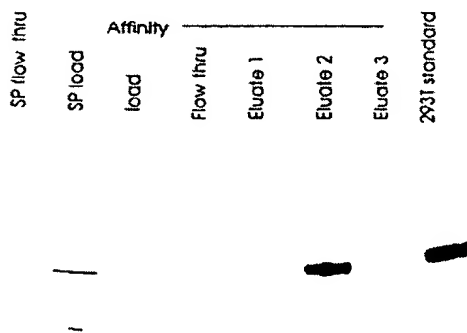


FIG. 8



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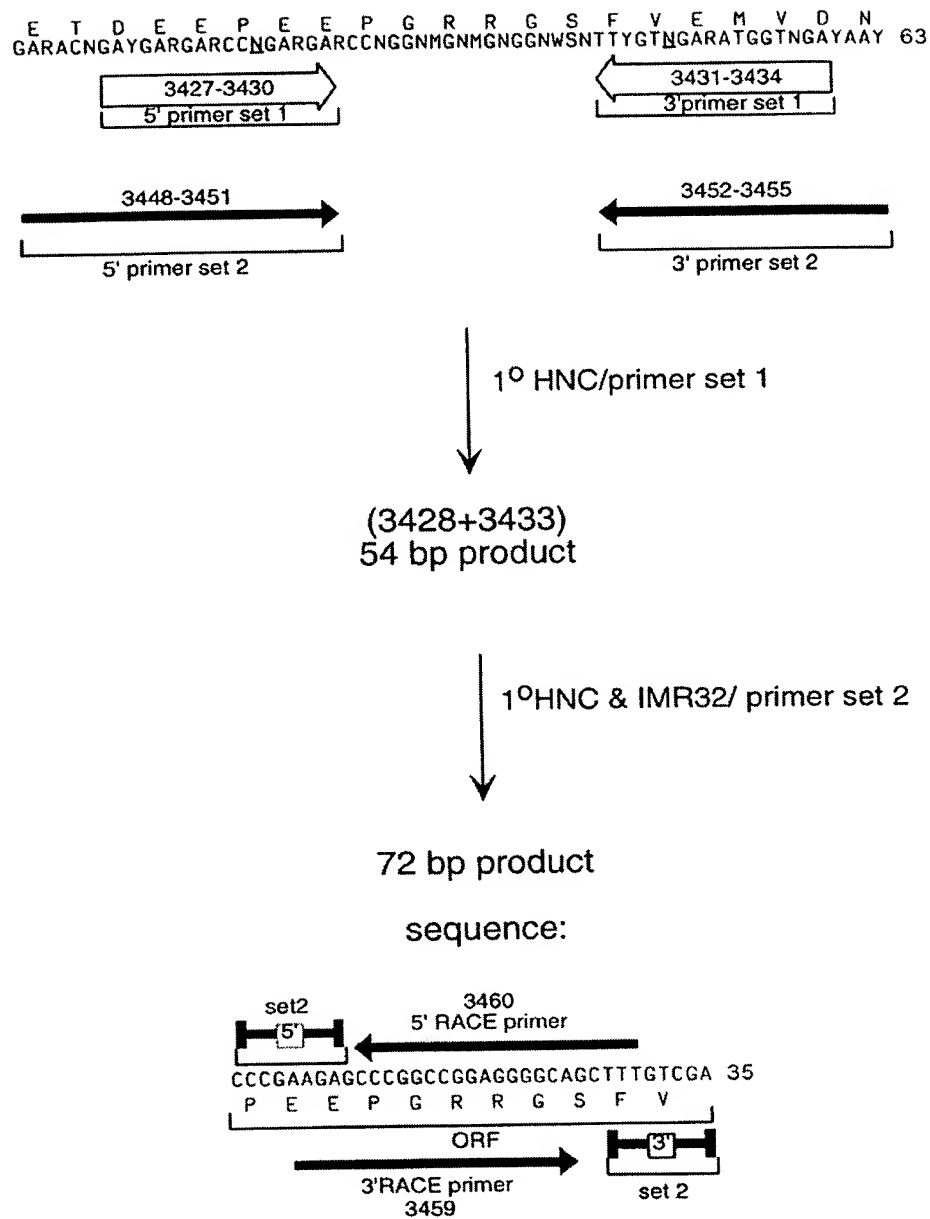


Fig. 9



## Replacement Sheet

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	10	20	30	40	
Hump501prot	M A Q A L P W L L L W M G A G V L P A H G T Q H G I R L P L R S G I G G A P I G	40			
Musp501prot	M A P A L H W L L L W V G S G M L P A Q G T H L G I R L P L R S G I A G P P L G	40			
	50	60	70	80	
Hump501prot	L R L P R E T D E E P E E P G R R G S F V E M V D N L R G K S G Q G Y Y V E M T	80			
Musp501prot	L R L P R E T D E E S E E P G R R G S F V E M V D N L R G K S G Q G Y Y V E M T	80			
	90	100	110	120	
Hump501prot	V G S P P Q T L N I L V D T G S S N F A V G A A P H P F L H R Y Y Q R Q I S S T	120			
Musp501prot	V G S P P Q T L N I L V D T G S S N F A V G A A P H P F L H R Y Y Q R Q I S S T	120			
	130	140	150	160	
Hump501prot	Y R D L R K G V Y V P Y T Q G K W E G E L G T D L V S I P H G P N V T V R A N I	160			
Musp501prot	Y R D L R K G V Y V P Y T Q G K W E G E L G T D L V S I P H G P N V I V R A N I	160			
	170	180	190	200	
Hump501prot	A A I T E S D K F F I N G S N W E G I L G L A Y A E I A R P D D S L E P F F D S	200			
Musp501prot	A A I T E S D K F F I N G S N W E G I L G L A Y A E I A R P D D S L E P F F D S	200			
	210	220	230	240	
Hump501prot	L V K Q T H V P N I F S L Q L C G A G F P L N Q S E V I A S V G G S M I I G G I	240			
Musp501prot	L V K Q T H I P N I F S L Q L C G A G F P L N Q T E A L A S V G G S M I I G G I	240			
	250	260	270	280	
Hump501prot	D H S L Y T G S L W Y T P I R R E W Y Y E V I I V R V E I N G Q D L K M D C K E	280			
Musp501prot	D H S L Y T G S L W Y T P I R R E W Y Y E V I I V R V E I N G Q D L K M D C K E	280			
	290	300	310	320	
Hump501prot	Y N Y D K S I V D S G T T N L R L P K K V F E A A V K S I K A A S S T E K F P D	320			
Musp501prot	Y N Y D K S I V D S G T T N L R L P K K V F E A A V K S I K A A S S T E K F P D	320			
	330	340	350	360	
Hump501prot	G F W L G E Q L V C W Q A G T T P W N I F P V I S L Y L M G E V T N Q S F R I T	360			
Musp501prot	G F W L G E Q L V C W Q A G T T P W N I F P V I S L Y L M G E V T N Q S F R I T	360			
	370	380	390	400	
Hump501prot	I L P Q Q Y L R P V E D V A T S Q D D C Y K F A I S Q S S T G T V M G A V I M E	400			
Musp501prot	I L P Q Q Y L R P V E D V A T S Q D D C Y K F A V S Q S S T G T V M G A V I M E	400			
	410	420	430	440	
Hump501prot	G F Y V V F D R A R K R I G F A V S A C H V H D E F R T A A V E G P F V T L D M	440			
Musp501prot	G F Y V V F D R A R K R I G F A V S A C H V H D E F R T A A V E G P F V T A D M	440			
	450	460	470	480	
Hump501prot	E D C G Y N I P Q T D E S T L M T I A Y V M A A I C A L F M L P L C L M V C Q W	480			
Musp501prot	E D C G Y N I P Q T D E S T L M T I A Y V M A A I C A L F M L P L C L M V C Q W	480			
	490	500			
Hump501prot	R C L R C L R Q Q H D D F A D D I S L L K	501			
Musp501prot	R C L R C L R H Q H D D F G D D I S L L K	501			

FIG. 10

FIG. 10



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CTGTTGGGCTCGCGGTTGAGGACAACTCTTCGCGGTCTTTCCAGTACTCT  
TGGATCGGAAACCCGTCGGCCTCCGAACGGTACTCCGCCACCGAGGGACCT  
GAGCGAGTCCGCATCGACCGGATCGGAAAACCTCTCGACTGTTGGGGTGAG  
TACTCCCTCTCAAAAGCGGGCATGACTTCTGCGCTAAGATTGTCAGTTTCC  
AAAAACGAGGAGGATTTGATATTCACCTGGCCCCGCGGTGATGCCTTTGAGG  
GTGGCCGCGTCCATCTGGTCAGAAAAGACAATCTTTTTGTTGTCAAGCTTG  
AGGTGTGGCAGGCTTGAGATCTGGCCATACACTTGAGTGACAATGACATCC  
ACTTTGCCCTTCTCTCCACAGGTGTCCACTCCCAGGTCCAAGTGCAGGTCCG  
ACTCTAGACCC

FIG. 11A

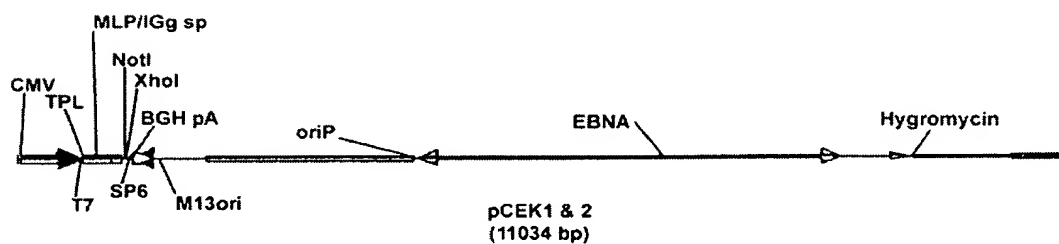


FIG. 11B





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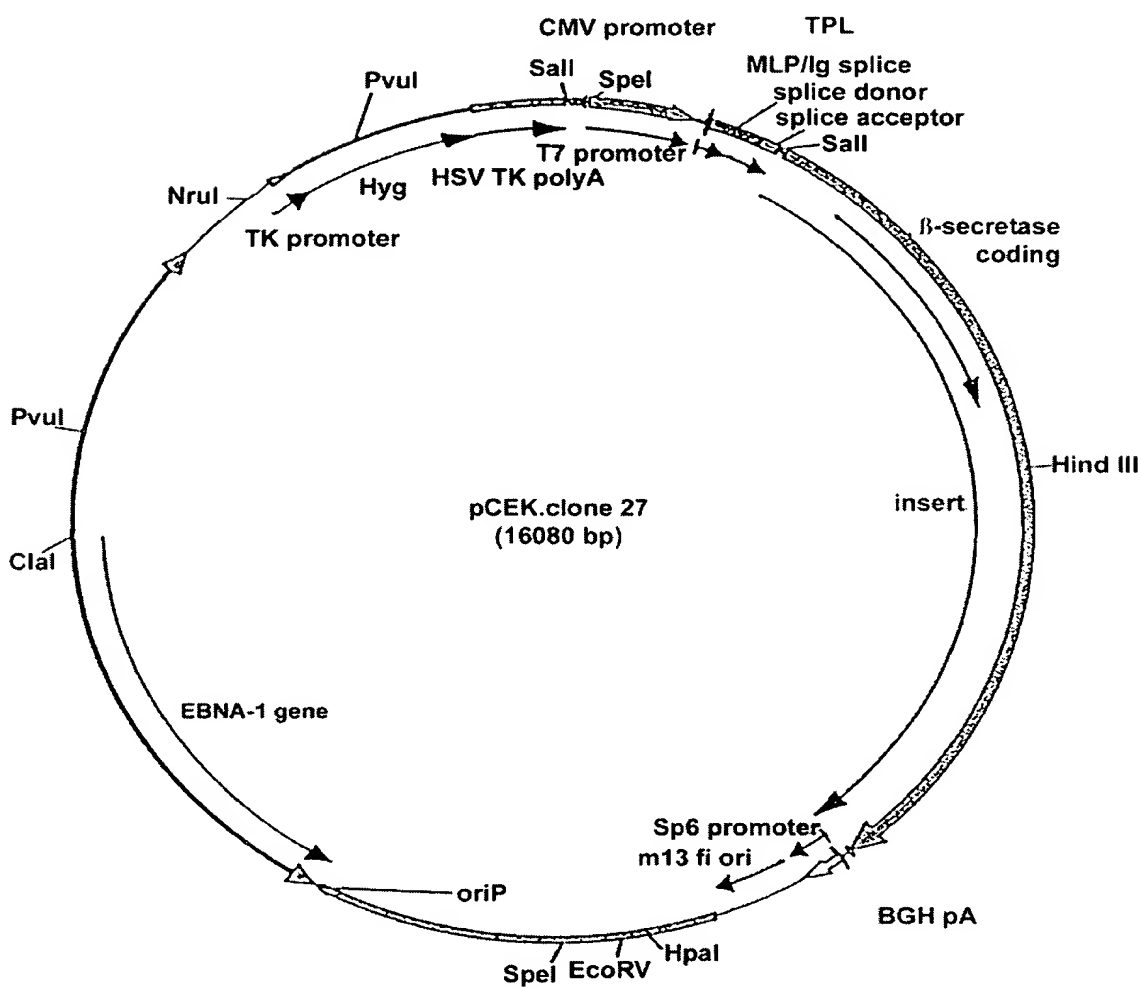


FIG. 12

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Figure 13A

ttctcatgtt tgacagctta tcatgcaga tccgggcaac gttgttgcat tgctgcaggc 60  
 gcagaactgg taggtatgga agatccgatg tacgggccag atatacgcgt tgacattgat 120  
 SpeI  
 tattgactag ttattaatag taatcaatta cgggggtcatt agttcatagc ccataatatgg 180  
agttccgcgt tacataactt acggtaaatg gccgcctgg ctgaccgcc aacgacccc 240  
gccattgac gtcaataatg acgtatgttc ccatagtaac gccaataggg actttccatt 300  
gacgtcaatg ggtggactat ttacggtaaa ctgccactt ggcagtacat caagtgtatc 360  
atatgccaag tacgccccct attgacgtca atgacggtaa atggcccgcc tggcattatg 420  
cccagtacat gaccttatgg gactttccta cttggcagta catctacgta ttagtcacg 480  
ctattaccat ggtgatgcgg ttttggcagt acatcaatgg gcgtggatag cggtttgact 540  
cacgggggatt tccaagtctc caccocattg acgtcaatgg gagtttgttt tggcaccaaa 600  
atcaacggga ctttccaaaa tgctgtaaca actccgccc attgacgcaa atgggcggta 660  
 ggcggtgtacg gtgggagggtc tataataagca gagctctctg gctaaactaga gaaccactg 720  
 ctactggct tatcgaaatt aatacgactc actataggga gacccaagct ctgttgggct 780



Figure 13B

cgcggttgag gaaaaactct tcgcggtctt tccagtactc ttggatcgga aaccgctcg 840

---

cctccgaacg gtactccgcc accgagggac ctgagcgagt ccgcatcgac cggatcggaa 900  
splice donor

aacctctga ctgttggggt gagtactccc tctcaaaagc gggcatgact tctgcgctaa 960

---

gattgtcagt ttccaaaaac gaggaggatt tgataattcac ctggcccgcg gtgatgcctt 1020

---

tgagggtggc cgcgtccatc tggtcagaaa agacaatctt tttgttgtca agcttgaggt 1080

---

gtggcaggct tgagatctgg ccatacactt gaggacaat gacatccact ttgccttctt 1140  
splice acceptor                      SalI

ctccacaggt gtccactccc aggtccaaact gcaggctcgac tctagacccg gggaattctg 1200

---

cagatatcca tcacactggc cgcactcgtc ccagcccgcg ccgggagctg cgagccgcga 1260

---

gctggattat ggtggcctga gcagccaacg cagccgcagg agcccggagc ccttgccccct 1320

---

gcccgcgcg cgcgccgcg gggggaccag ggaagccgc accggcccgc catgcccgc 1380

---

cctcccagcc ccgcccggag ccgcgcgccg ctgcccaggc tggccgcgcg cgtgccgatg 1440

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tagcgggctc cggatcccag cctctccccct gctccccgtg tctgcggatc tcccctgacc 1500

---

gctctccaca gcccggaacc gggggctggc ccagggccct gcaggcccctg gcgtcctgat 1560

---

gcccccaagc tccctctctt gagaagccac cagcaccacc cagacttggg ggcaggcgcc 1620



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Figure 13C

1677	agggacggac gtgggccagt gcgagcccag agggcccgaaggccggggcc cacc atg Met
	<u>1</u>
1725	gcc caa gcc ctg ccc tgg ctc ctg ctg tgg atg ggc gcg gga gtg ctg Ala Gln Ala Leu Pro Trp Leu Leu Trp Met Gly Ala Gly Val Leu
	5 10 15
1773	cct gcc cac gcc acc cag cac ggc atc cgg ctg ccc ctg cgc agc ggc Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser Gly
	20 25 30
1821	ctg ggg gcc gcc ccc ctg ggg ctg cgg ctg ccc cgg gag acc gac gaa Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp Glu
	35 40 45
1869	gag ccc gag gag ccc gcc cgg cgg agg ggc agc ttt gtg gag atg gtg gac Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val Asp
	50 55 60 65
1917	aac ctg agg gcc aag tcg ggg cag gcc tac tac gtg gag atg acc gtg Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr Val
	70 75 80
1965	ggc agc ccc ccg cag acg ctc aac atc ctg gtg gat aca ggc agc agt Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser Ser
	85 90 95





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Figure 13E

ctc ttc tcc ctg cag ctt tgt ggt gct ggc ttc ccc ctc aac cag tct Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser 210 215 220 225	2349
gaa gtg ctg gcc tct gtc gga ggg agc atg atc att gga ggt atc gac Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp 230 235 240	2397
cac tcg ctg tac aca ggc agt ctc tgg tat aca ccc atc cgg cgg gag His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu 245 250 255	2445
tgg tat tat gag gtc atc att gtg cgg gtg gag atc aat gga cag gat Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp 260 265 270	2493
ctg aaa atg gac tgc aag gag tac aac tat gac aag agc att gtg gac Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp 275 280 285	2541
agt ggc acc acc aac ctt cgt ttg ccc aag aaa gtg ttt gaa gct gca Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala 290 295 300 305	2589
gtc aaa tcc atc aag gca gcc tcc tcc acg gag aag ttc cct gat ggt Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly 310 315 320	2637



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Figure 13F

2685	ttc tgg cta gga gag cag ctg gtg tgc tgg caa gca ggc acc acc cct Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro 325 330 335
2733	tgg aac att ttc cca gtc atc tca ctc tac cta atg ggt gag gtt acc Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr 340 345 350
2781	aac cag tcc ttc cgc atc acc atc ctt ccg cag caa tac ctg cgg cca Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro 355 360 365
2829	gtg gaa gat gtg gcc acg tcc caa gac gac tgt tac aag ttt gcc atc Val Glu Asp Val Ala Thr Ser Gln Asp Cys Tyr Lys Phe Ala Ile 370 375 380 385
2877	tca cag tca tcc acg ggc act gtt atg gga gct gtt atc atg gag ggc Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly 390 395 400
2925	ttc tac gtt gtc ttt gat cgg gcc cga aaa cga att ggc ttt gct gtc Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val 405 410 415
2973	agc gct tgc cat gtg cac gat gag ttc agg acg gca gcg gtg gaa ggc Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly 420 425 430



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Figure 13G

cct ttt gtc acc ttg gac atg gaa gac tgt ggc tac aac att cca cag Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro Gln 435 440 445	3021
aca gat gag tca acc ctc atg acc ata gcc tat gtc atg gct gcc atc Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ile 450 455 460 465	3069
tgc gcc ctc ttc atg ctg cca ctc tgc ctc atg gtg tgt cag tgg cgc Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp Arg 470 475 480	3117
tgc ctc cgc tgc ctg cgc cag cag cat gat gac ttt gct gat gac atc Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp Ile 485 490 495	3165
tcc ctg ctg aag tga ggaggcccat gggcagaaga tagagattcc cctggaccac Ser Leu Leu Lys 500	3220
acctccgtgg ttcactttgg tcacaagtag gagacacaga tggcacctgt ggcagagca cctcaggacc ctcccaccc accaaatgcc tctgcctga tggagaagga aaaggctggc aaggtagggtt ccagggactg tacctgtagg aaacagaaaa gagaagaag aagcactctg ctggcgggaa tactcttggt cacctcaaat ttaagtcggg aaattctgct gcttgaaact	3280 3340 3400 3460





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Figure 13H

tcagccctga acctttgtcc accattcctt taaattctcc aacccttctt attcttcttt 3520

tcttagtttc agaagtactg gcatcacacg caggttacct tggcgtgtgt ccctgtggtg 3580

HindIII

ccctggcaga gaagagacca agcttggttc cctgctggcc aaagtcagta ggagaggatg 3640

cacagtttgc tatttgcttt agagacaggg actgtataaa caagcctaac attggtgcaa 3700

agattgcctc ttgaattaaa aaaaaaact agattgacta tttatacaaa tgggggcggc 3760

tggaaaagagg agaaggagag ggagtacaaa gacaggggaat agtgggatca aagctaggaa 3820

aggcagaaac acaaccactc accagtcccta gttttagacc tcattctccaa gatagcatcc 3880

catctcagaa gatgggtgtt gttttcaatg ttttctttc tgtggttgca gcctgaccaa 3940

aagtgagatg ggaaggggctt atctagccaa agagctcttt tttagctctc ttaaatgaag 4000

tgccactaa gaagttccac ttaacacatg aatttctgcc atattaattt cattgtctct 4060

atctgaacca ccctttattc tacatatgat aggcagcact gaaatatcct aacccctaa 4120

gctccagggtg ccctgtggga gagcaactgg actatagcag ggctgggctc tgtcttcttg 4180

gtcataggct cactctttcc cccaaatctt cctctggagc tttgcagcca aggtgctaaa 4240

aggaataggt aggagacctc ttctatctaa tccttaaaag cataatgttg aacattcatt 4300



Figure 13I

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caagatcttt acataattca gagtgggttc attgccttcc taccctctct aatggcccct 4420  
ccatttattt gactaaagca tcacacagtg gcactagcat tataccaaga gtatgagaaa 4480  
tacagtgcct tatggctcta acattactgc cttcagtatc aaggctgcct ggagaaaagg 4540  
tggcagcctc agggcttctc tatgtcctcc accacaagag ctcttctgat aaggtcatct 4600  
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ataagggaga gggaaataca aggagggcct ctggtgttcc tggcctcagc cagctgccca 4900  
caagccataa accaataaaa caagaatact gagtcaagttt tttatctggg ttctcttcat 4960  
tcccactgca ctggtgtctg ctttgggtga ctgggaacac ccataaata cagagtctga 5020  
caggaagact ggagactgtc cacttctagc tcggaactta ctgtgtaaat aaactttcag 5080  
aactgctacc atgaagtga aatgccacat tttgctttat aattctacc catgttggga 5140



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Figure 13J

aaaactggct ttttccagc ctttccagg gcataaaact caacccttc gatagcaagt 5200  
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tgcttgtaaa aatatgtatt atacatctgt atttttaaat tctgctcctg aaaaatgact 5380  
gtccattct ccaactcactg catttggggc ctttccatt ggtctgcatg tcttttatca 5440  
ttgcaggcca gtggacagag ggagaaggga gaacaggggt cgccaacact tgtgttgctt 5500  
tctgactgat cctgaacaag aaagagtaac actgaggcgc tcgctcccat gcacaaactct 5560  
ccaaaacact taccctcctg caagagtggg ctttccgggt ctttactggg aagcagttaa 5620  
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cctttcctgt tcatgacagc tactaacctg gagacagtaa catttcatta accaaagaaa 5920  
gtgggtcacc tgacctctga agagctgagt actcaggcca ctccaatcac cctacaagat 5980

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Figure 13K

gccaaaggagg tccaggaag tccagctct taaactgacg ctagtcaata aacctgggca 6040  
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aaagacggaa aagagtatca aaggcagaaa ggagatcatt tagttgggtc tgaaaggaaa 6160  
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gactgtgcct tctagttgcc agccatctgt tgtttgcccc tccccgtgc ctctcttgac 6400  
cctggaaggt gccactccca ctgtccttct ctaataaaat gaggaatgt catcgcatgt 6460  
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ggcgggtgtg gtgggttacgc gcagcgtgac cgctacactt gccagcgccc tagcgccgc 6700  
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Figure 13L

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HpaI  
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Figure 13M

tgggggtcagg attccacgag ggtagtgaac catttttagtc acaaggggcag tggctgaaga 7720

tcaaggagcg ggcagtgaac tctcctgaat cttcgcctgc ttcttcattc tccttcgttt 7780

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aggtttcagg tgacgcccc agaataaaat ttggacgggg ggttcagtggtg tggcattgtg 7900

ctatgacacc aatataaacc tcacaaacc cttgggcaat aaatactagt gtaggaatga 7960

SpeI

aacattctga atatctttaa caatagaaat ccatgggggtg gggacaaagcc gtaaagactg 8020

gatgtccatc tcacacgaat ttatggctat gggcaacaca taatcctagt gcaatatgat 8080

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ctctaacacc cccgaaaatt aaacgggggt cccgcaccaat ggggcccata acaaaagaca 8260

agtggccact cttttttttg aaattgtgga gtggggggcac gcgtcagccc ccacacgccg 8320

ccctgcgggtt ttggactgta aaataagggt gtaataactt ggctgattgt aaccccgcta 8380

accactgcgg tcaaaaccact tgcccacaaa accactaatg gcacccccgg gaataacctg 8440

ataagtaggt gggcggggcca agataggggc gcgattgctg gacaaattac 8500



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Figure 13N

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gctatccctaa tctatatctg gtagcatat gctatccctaa tctatatctg gtagtatat 9040  
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oriP  
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Figure 130

tctgattgct caccaggtaa atgtcgctaa tgttttccaa cgcgagaagg tgttgagcgc 9400

ggagctgagt gacgtgacaa catgggtatg cccaattgcc ccatgttggg aggacgaaaa 9460

tggtgacaag acagatggcc agaaatacac caacagcacg catgatgtct actggggatt 9520

tattctttag tgcgggggaa tacacggctt ttaatacgat tgagggcgct tcctaacaag 9580

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gccattccaa aggggagacg actcaatggt gtaagacgac attgtggaat agcaagggca 9940

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accaagtcc ctctgtcgggt agtcctttct acgtgactcc tagccaggag agctcttaaa 10060

ccttctgcaa tgttctcaaa ttctgggttg gaacctcctt gaccacgatg cttccaac 10120

cacctcctt ttttgcgct gcctccatca ccctgacccc ggggtccagt gcttgggcct 10180





Figure 13P

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Figure 13Q

cctgcccctc ctctgtctcc tggccctctct gcccctctctc ctgtctctgc cctctctctc 11080  
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ctgagcctca agccaggcct caaattctc gtccccctt ttgctggacg gtagggatgg 11800  
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Figure 13R

ClalI

aacggaagaa aagctgggtg cggcctgtga ggatcagctt atcgatgata agctgtcaaa 11920

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PvuI



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Figure 13S

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Figure 13T

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NruI

Figure 13U

aaccccgccc agcgtcttgt cattggcgaa ttcgaacacg cagatgcagt cggggcgggcg 14440  
cgttcccagg tccacttcgc atattaaggt gacgcgtgtg gcctcgaaca ccgagcgacc 14500  
ctgcagcgac ccgcttaaca gcgtcaacag cgtgccgcag atccccgggca atgagatatg 14560  
aaaaagcctg aactcacccg cactctgtgc gagaagtctc tgatcgaaaaa gttcgacagc 14620  
gtctccgacc tgatgcagct ctcgaggggc gaagaaatctc gtgctttcag cttcgatgta 14680  
ggaggggcgtg gatatgtcct gcgggtaaat agctgcgccg atgggtttcta caaagatcgt 14740  
tagtgggata ggcaattgc atcgccgcgc ctccccgatt ccggaagtgc ttgacattgg 14800  
ggaattcagc gagagcctga cctattgcat ctcccgccgt gcacaggggtg tcacgttgca 14860  
agacctgcct gaaaccgaac tgcccgcgtgt tctgcagccg gtcgcggagg ccatggatgc 14920  
PvuI  
gacgcgtgcg gccgatctta gccagacgag cgggttcggc ccattcggac cgcaagggaat 14980  
cgggtcaatac actacatggc gtgatttcat atgcgcgatt gctgatcccc atgtgtatca 15040  
ctggcaaaact gtgatggacg acaccgtcag tgcgtccgtc gcgcaggctc tcgatgagct 15100  
gatgtcttgg gccgaggact gccccgaagt ccggcacctc gtgcacgcgg atttcggctc 15160  
caacaatgct ctgacggaca atggccgcat aacagcggtc attgactgga gcgagcgcat 15220

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Figure 13V

gttcggggat tccaatacg aggtcgccaa catctttctt tggaggccgt ggttggcggg 15280  
tatggagcag cagacgcgct acttcgagcg gaggcatacc gagcttgca gatacgccgcg 15340  
gctccgggcg tatatgctcc gcatttgtct tgaccaactc tatcagagct tggttgacgg 15400  
caatttcgat gatgcagctt gggcgagggg tcgatgcgac gcaatcgtcc gatccggagc 15460  
cgggactgtc gggcgctacac aaatcgcccg cagaagcgcg gccgtctgga ccgatggctg 15520  
tgtagaagta ctgcgccgata gtggaaacgg gagatggggg aggctaactg aaacacggaa 15580  
ggagacaata ccggaaggaa ccgcgcctat gacggcaata aaaagacaga ataaaacgca 15640  
cgggtgttgg gtcgtttgtt cataaacgcg ggggtcggtc ccagggctgg cactctgtcg 15700  
ataccacc gagaccccat tggggccaat acgcccgcgt ttcttctt tcccccccc 15760  
accccccaag ttcgggtgaa ggcccagggc tcgcagccaa cgtcggggcg gcaggccctg 15820  
ccatagccac tggccccgtg ggtagggac ggggtcccc atgggggaatg gtttatggtt 15880  
cgtgggggtt attattttg gcgttcgctg ggggtctggtc cacgactgga ctgagcagac 15940  
agacccatgg tttttggatg gcctgggcat ggaccgcatg tactggcgcg acacgaacac 16000  
cgggcgtctg tggctgccaa acacccccga cccccaaaa ccaccgcgcg gatttctggc 16060



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Figure 13W  
SallI  
gtgccaagct agtcgaccaa  
↑

16080





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CTGTTGGGCTCGCGGTTGAGGACAAACTCTTCGCGGTCTTTCCAGTACTCTTGGATCGGAAAC  
CCGTCGGCCTCCGAACGGTACTCCGCCACCGAGGGACCTGAGCGAGTCCGCATCGACCGGAT  
CGGAAAACCTCTCGACTGTTGGGGTGAGTACTCCCTCTCAAAAAGCGGGCATGACTTCTGCGCT  
AAGATTGTCAGTTTCAAAAAACGAGGAGGATTTGATATTCACCTGGCCCCGCGGTGATGCCTTT  
GAGGGTGGCCCGCTCCATCTGGTCAGAAAAGACAATCTTTTTGTTGTCAAGCTTGAGGTGTGG  
CAGGCTTGAGATCTGGCCATACACTTGAGTGACAATGACATCCACTTGCCTTTCTCTCCACAG  
GTGTCCACTCCCAGGTCCAACCTGCAGGTCGACTCTAGACCC

FIG. 14A

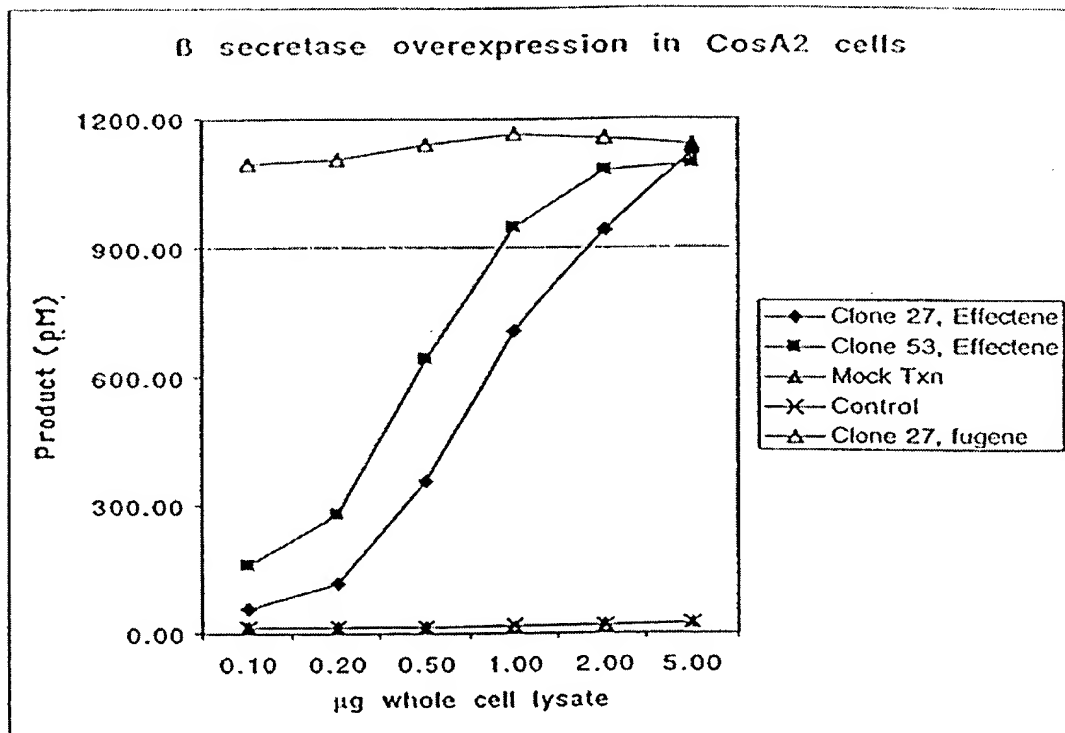


FIG. 14B



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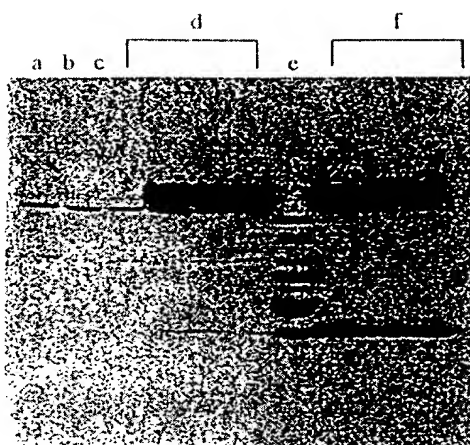


FIG. 15A

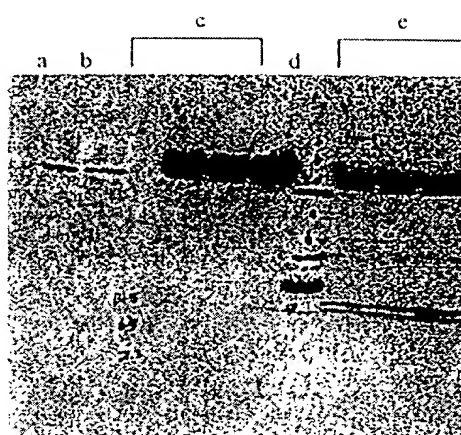


FIG. 15B



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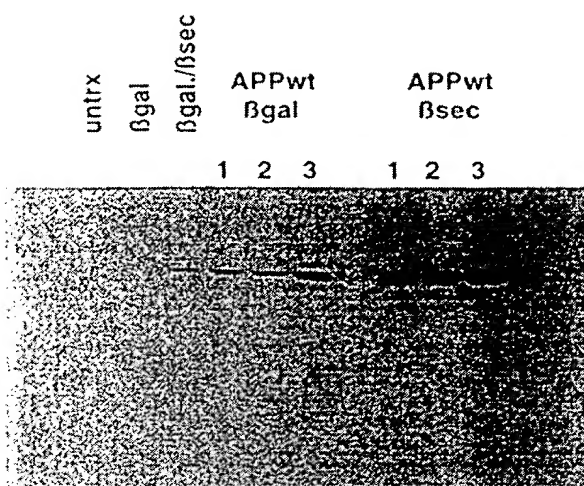


FIG. 16A

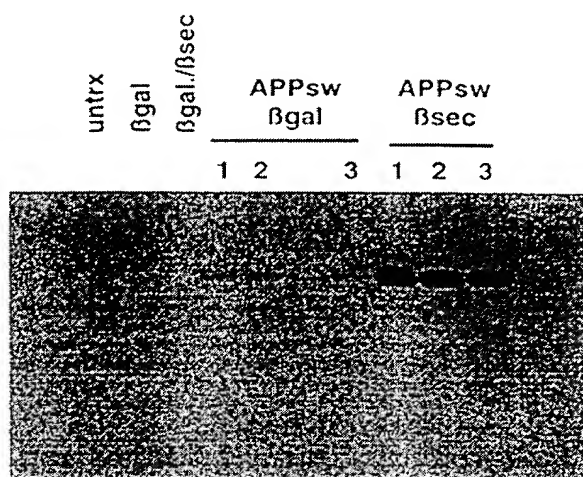


FIG. 16B



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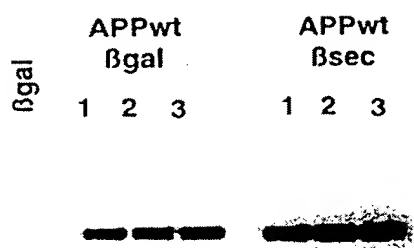


FIG. 17A

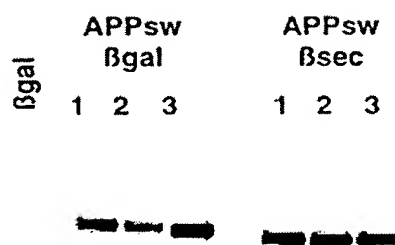
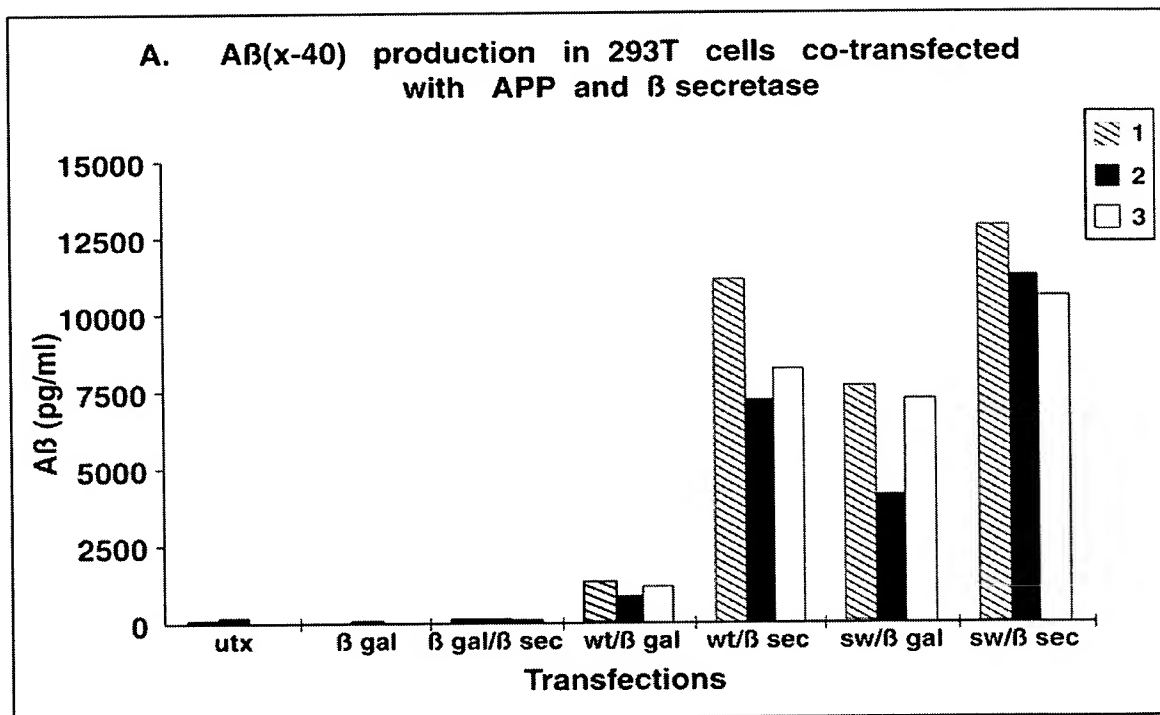


FIG. 17B



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**Fig. 18**



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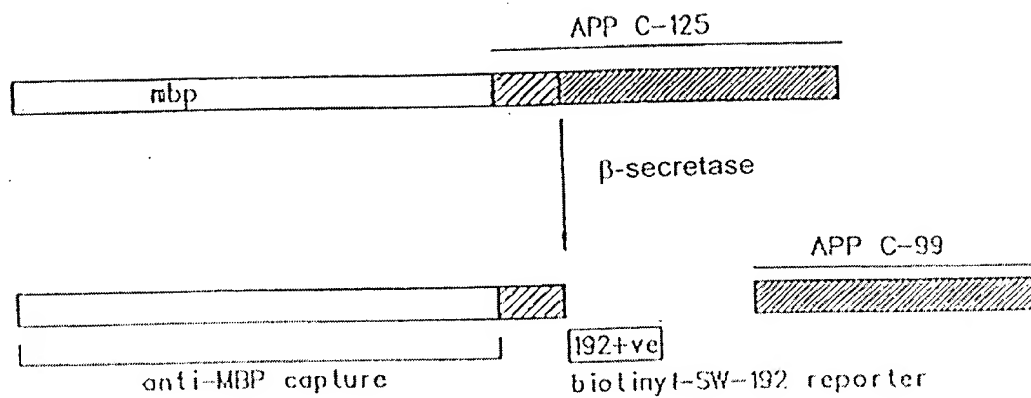


FIG. 19A

Wild-Type Sequence	...Val-Lys-Met-Asp...
Swedish Sequence	...Val-Asn-Leu-Asp...

FIG. 19B

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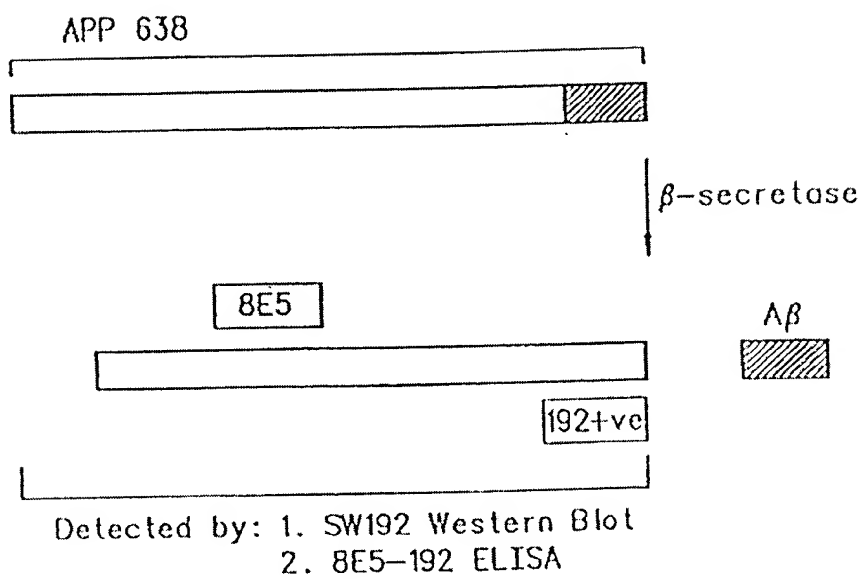


FIG. 20



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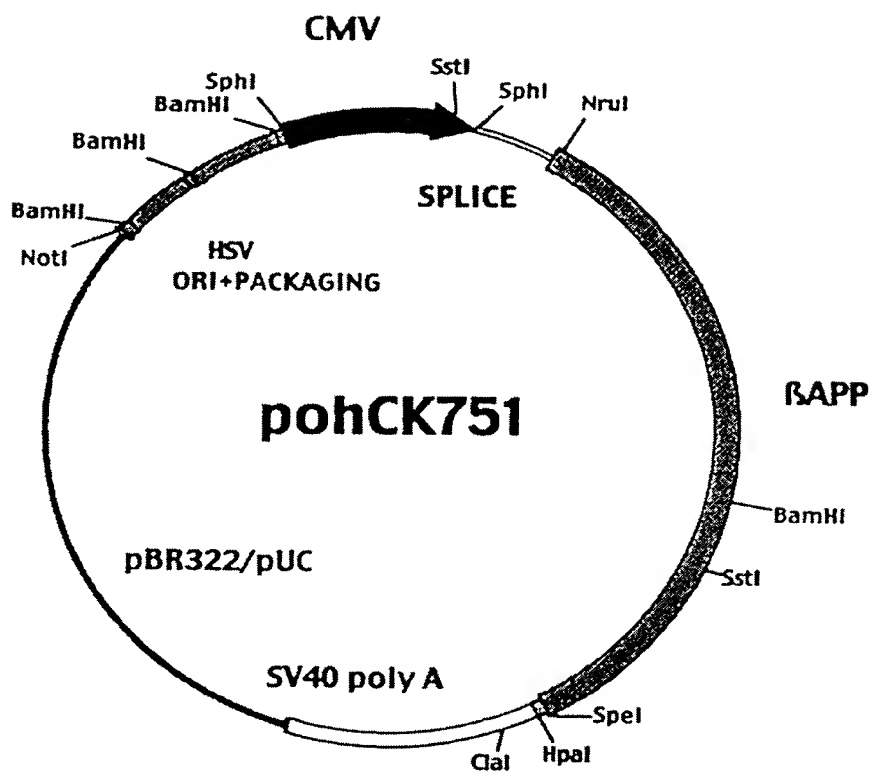


FIG. 21